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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 05/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/478,263	JARRELL ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Request for Continued Examination (RCE)

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/25/05 has been entered. Claims 1-3 and 5-23 were pending. No claims were added, canceled or amended. Therefore, claims 1-3 and 5-23 are currently pending. An action on the merit follows.

Those sections of Title 35, US code, not included in the instant action can be found in previous office actions.

Withdrawn Objections and/or Rejections

2. All rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claim Rejections - 35 USC § 112

3. Claims 1-3 and 5-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the claimed invention (e.g., see *In re Edwards*, 568 F.2d 1349, 1351-52, 196 USPQ 465, 467 (CCPA 1978)). Applicants' claims are directed to a broad genus of methods for the combinatorial biosynthesis of unspecified compounds. Here, Applicants provide no structural limitations for the "starter units", "handles" and "solid supports" used in conjunction with the method. In addition, Applicants biosynthetic enzymatic machinery includes an unknown number of enzymes and/or enzymatic machinery system constituents drawn to the modified polyketide synthetases, natural and modified peptide synthetases, natural and modified terpene synthases and natural and modified animal fatty acid synthases (e.g., see newly amended claim 1). Furthermore, no limitations are provided for the "synthetic organic chemistry" that is further used to diversify the biosynthetic products (e.g., see claim 1, step d). Thus, Applicants are claiming virtually an infinite number of methods for producing virtually an infinite number of compounds that may or may not be useful.

In contrast, Applicants' specification does not even provide a single working example (i.e., no *quid pro quo* here). Although, Applicants' specification provides a limited number starter units, handles and solid supports that could "potentially" be used in the claimed method (e.g., see figures), the evidence suggests that these experiments were never performed. In support of this position the Examiner notes that no biological activities and/or physical characterization is presented in the specification for any

compounds that might otherwise indicate the success and/or failure of the claimed method.

Applicants are referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding adequate disclosure. For adequate disclosure, like enablement, requires ***representative examples***, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that *applicant had possession of the full scope of the claimed invention.* See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure. In addition, when there is ***substantial variation within the genus***, one must describe a sufficient variety of species to reflect the variation within the genus (e.g., see MPEP § 2163.05).

Here, the variation within the genus would be enormous because no limitations have been placed on the starter units, handles and/or solid phase resins. Furthermore, no limitations have been placed on the type of synthetic organic chemistry that would subsequently be employed to further modify the compounds. In addition, a review of the literature indicates that combinatorial biosynthesis is a new and highly unpredictable field that requires identification/characterization of the "modular biosynthetic enzymatic machinery." With the exception of polyketides and nonribosomally produced peptides

and carbohydrates, this has not been done. For example, Taylor states that for the biosynthesis of epothione would require a mixed NRPS/PKS "biosynthetic enzymatic machinery." However, Taylor states that there are currently "no examples of such an approach [in the literature]" and that while it may be "easy to imagine how novel epothione analogs could be generated", "[m]uch work remains to be done in elucidating the organization and structure of hybrid PKSs/NRPSs, however, before combinatorial biosynthesis with these systems can be undertaken" (emphasis added) (see Taylor, S. V. in "Handbook of Combinatorial Chemistry" Eds. Nicolaou, K. C.; Hanko, R.; Hartwig, W. Weinheim Germany: Wiley-VCH 2002, Vol. 2, page 1075, last paragraph). In addition, Darby states that enzymatic synthesis in general is severely limited by that enzymes narrow substrate specificity and, as a result, it is unclear whether Applicants claimed starter units, functional handles, etc. would even act as substrates for the vast majority of enzymes in those enzymatic pathways (e.g., see Dalby, page 1, lines 15-20, "However, the use of enzymes in the synthesis of complex molecules is currently hindered by the time taken to discover or develop an enzyme with the required substrate specificity ... identifying a suitable biocatalyst is ***extremely difficult***, as the known enzymes often do not show activity towards the desired substrate"; see also lines 27-28, "it is much more difficult to find an ... enzyme with activity towards a particular substrate, due to the high substrate specificity exhibited by most natural enzymes"; see also page 17, paragraph 1 wherein the narrow substrate specificity for transketolase is set forth that would presumably fall within the scope of Applicants' claims because it is useful in producing polyketides). Therefore, even a greater showing would be required to

reflect the variation within the genus in accordance with MPEP § 2163.05, which has not been done.

Furthermore, it should be noted that Applicants never claim a "screening" step that would otherwise allow a person of skill in the art to sort through and find a "useful" compound and/or library from the large number of compounds that would unquestionably result from the claimed method (i.e., no "screening step" is provided in any of the current claims). In *University of Rochester v. G.D. Searle & Co., Inc.* (U.S. Court of Appeals Federal Circuit (CAFC) 358 F.3d 916, 69 USPQ2d 1886 (Fed.Cir.2004)), a method for selectively inhibiting PGHS-2 enzymatic activity failed to meet the written description requirement because the patent "neither disclose[d] any such compound nor provide[d] any suggestion as to how such a compound could be made or otherwise obtained other than by trial-and-error research." *Id.* at 2 (quoting *University of Rochester versus G.D. Searle and Co., Inc.*, 249 F.Supp.2d at 220). Here, Applicants have similarly failed to disclose any "useful" compounds and/or libraries (e.g., no biological activities have been set forth in the specification). Consequently, any method for producing such a library would likewise be defective because that library would still need to be screened by "trial-and-error" methods to determine whether it was useful. Thus, Applicants have not disclosed any methods for producing a library of compounds that would not require "trial-and-error" screening in violation of *Rochester*.

Finally, The CAFC has also stated that a "written description on an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject

matter sufficient to distinguish it from other materials." (e.g., see *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993)). Here, Applicants have failed to provide a definition, structure, formula or chemical name for any of the "starter units", "handles", "template structures", etc. that fall within the scope of Applicants' claims. In addition, the CAFC has stated that a genus, which is set forth only in functional terms, "... is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function" (e.g., see *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1406 (1997)). Here, Applicants' "starter units", "handles", "template structures", etc. can only be distinguished from other compounds by their function (e.g., the ability of the starter units to react with the biosynthetic enzymatic machinery), which was held to be impermissible in *Lilly*. Just as the generic term "cDNA" did not provide an adequate written description for the broad class of mammalian or vertebrate insulin DNA in *Lilly*, neither does the generic terms "starter unit", "handle" or "template structure" provide an adequate written description for the broad class of currently claimed compounds that react with the biosynthetic enzymatic machinery because these terms only defines what the compounds can do (e.g., the ability of a "starter unit" to react with biosynthetic enzymatic machinery) rather than what the compounds are (e.g., chemical formulas). In fact, this case is even more egregious than *Lilly* because there is no "genetic code" to correlate the starter units, for example, with the enzymatic machinery.

Response

4. Applicant's arguments directed to the above written description rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants argue, "the recitation of particular biosynthetic enzymatic machinery systems limits the universe of potential starter units significantly" and, as a result, the claims are presumably not as broad as the Examiner contends (e.g., see 11/25/05 Response, pages 2-4, especially paragraph bridging pages 3 and 4).

[2] Applicants argue, "regarding the recited handles and solid supports ... Applicant has disclosed properties that a solid support should have to be useful in the claimed methods. For example, the specification states that solid supports should have a functional group that can bind to a handle on a starter unit, such as an alkyne olefin or iodoalkene" (e.g., see 11/25/05 Response, page 4, paragraphs 2 and 3).

[3] Applicants argue, "[t]he relevant question is not whether each and every family member of each recited biosynthetic enzymatic machinery system is disclosed. Rather, the relevant question is whether one skilled in the art would understand from the specification that the inventors were in possession of the claimed invention at the time of filing ... The answer to this question is clearly 'yes'." (e.g., see 11/25/05 Response, paragraph bridging pages 4 and 5).

[4] Applicants argue, "One skilled in the art would be able to easily identify family members of any of the recited biosynthetic enzymatic machinery systems based on any number

of factors including structural and/or sequence identity or similarity to known members of each family, conservation of the catalytic core and whether the enzyme in question is functionally similar in that it catalyzes the reaction common to the family" (e.g., see 11/25/05 Response, page 5, paragraph 1).

[5] Applicants argue, "the Examiner is incorrect in the assertion that no limitations are provided for the synthetic organic chemistry that is further used to divers[ify] tee biosynthetic products. On page 14, lines 14-27, Applicants disclose that template structures can be functionalized using nucleophilic addition ... and nitrile oxide cycloaddition" (e.g., see 11/25/05 Response, page 5, second to last paragraph).

[6] Applicants argue, "One skilled in the art would be ale to choose which functionalization reaction or reactions to employ in a given combinatorial biosynthesis based on the starter units provided and the biosynthetic enzymatic machinery systems utilized ... the practitioner is limited to those functionalization reactions that are capable of acting on the product of the combinatorial biosynthesis product. As such, the universe of potential synthetic organic chemistry reactions that may be used on any given combinatorial biosynthesis product is limited" (e.g., see 11/25/05 Response, paragraph bridging pages 5 and 6).

[7] Applicants argue, "it was well within the knowledge and capability of one skilled in the art at the time the application was filed to subject a given substrate, which substrate is initially chosen by the practitioner, to an appropriate biosynthetic enzyme. Applicant discloses several enzyme/substrate combinations merely as examples ... Applicant has not asserted that any particular enzyme/substrate combination or combinations is a critical feature of the claimed invention ... Rather, methods of the invention encompass the concept that diverse compounds

can be synthesized using a combination of enzymatic reactions and organic chemistry ... Thus, the description of methods for the combinatorial biosynthesis of one or more compounds comprising both enzymatic reactions and organic chemistry reactions must be read from the point of view of one skilled in the art, that is, from the point of view of those who are already knowledgeable about specific enzymatic and/or organic chemistry techniques" (e.g., see 11/25/05 Response, paragraph bridging pages 6 and 7).

[8] Applicants argue, "[a]s the Examiner is surely aware, disclosure of working examples ... is not necessary" and cite MPEP §2164.05(a) and In re Buchner in support of this position (e.g., see 11/25/05 Response, page 7, first full paragraph).

[9] Applicants argue, "the claims at issue in Rochester are very different from those pending in the instant application, and therefore the reasoning in Rochester is not directly applicable ... The claims in *Rochester* were directed to methods comprising administration of specific compound with a specific activity, i.e., selectively inhibiting PGHS-2 activity. The specification did not disclose any compound with this activity, but merely methods that could be used to make such a compound ... In contrast, the claims in the instant application ... do not recite the synthesis of any particular compound nor do they recite that any of the synthesized compounds must have any particular activity" (e.g., see 11/25/05 Response, pages 7 and 8, "Screening Step" section).

This is not found persuasive for the following reasons:

[1] First, the Examiner notes that Applicants provide no evidence to support this statement. Second, even if, *assuming arguendo*, the recitation of particular biosynthetic enzymatic machinery "significantly" limited the starter units that could be used the claims would

still encompass an infinite number of compounds (i.e., a tiny fraction of an infinite number is still an infinite number). Third, Applicants have failed to address the Taylor and Dalby references that show that the art is unpredictable and as a result, it is not even possible to determine how many compounds might be encompassed by the claims. Fourth, when there is little to no disclosure in the instant specification of the starting material or conditions under which claimed process can be carried out (which is the case here), this failure cannot be rectified by asserting that all disclosure related to the process is within skill of art. *Genentech Inc. v. Novo Nordisk A/S* (CA FC) 42 USPQ2d 1001 (3/13/1997).

[2] Applicants arguments are not commensurate in scope with the claims. Claim 1, for example, does not require that the claimed solid supports contain functional groups that can bind alkynes, olefins or iodoalkenes. Furthermore, the language in the cited passages (e.g., pages 8 and 9) is merely "exemplary" and, as a result, no patentable "limitation" has been set forth.

[3] The Examiner agrees that the test for sufficiency of support is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession [of the invention] at the time of the later claimed subject matter" (see *Ralston Purina Co. v. Far-Mar-Co.*, 772 F.2d 1570, 1575, 227 U.S.P.Q. 177, 179 (Fed. Cir. 1985)) and has never argued for anything else. However, the number of disclosed examples/species in making this determination and, as outlined above, indicates that Applicants were not in possession of the claimed invention.

[4] This statement is entirely unsupported. Applicants do not provide any evidence that the currently claimed biosynthetic enzymatic machinery contains a "common core" structure of sequence homology. That is, Applicants' arguments do not rise to the level of factual evidence.

See MPEP § 716.01(c): The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Furthermore, Applicants failed to address the Taylor and Dalby references, which show that the art is unpredictable.

[5] Applicants arguments are not commensurate in scope with the claims. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Here, Applicants' independent claim 1, for example, does not require nucleophilic addition, nitrile oxide cycloaddition, or any other reaction set forth in the cited passage and, as a result, Applicants' arguments are moot. Furthermore, the cited reactions are merely "exemplary" and would not restrict the claimed scope even if these limitations were to be, for the sake of argument, impermissibly read into the claims.

[6] Again, when there is little to no disclosure in the instant specification of the starting material or conditions under which claimed process can be carried out, this failure cannot be rectified by asserting that all disclosure related to the process is within skill of art. *Genentech Inc. v. Novo Nordisk A/S* (CA FC) 42 USPQ2d 1001 (3/13/1997). Furthermore, whatever limitations that might result from the use of an unknown, unspecified, as yet to be determined combinatorial biosynthesis product would not limit the universe to anything less than an infinite number of compounds because, as mentioned above, a fraction of an infinite number is still an infinite number.

[7] Again, when there is little to no disclosure in the instant specification of the starting material or conditions under which claimed process can be carried out, this failure cannot be

rectified by asserting that all disclosure related to the process is within skill of art. *Genentech Inc. v. Novo Nordisk A/S* (CA FC) 42 USPQ2d 1001 (3/13/1997). Furthermore, Applicants have failed to address the Taylor and Darby references which show that the art is unpredictable and, as a result, an even greater disclosure would be required by Applicants. See MPEP § 2163 ("In contrast, for inventions in emerging and unpredictable technologies, or for inventions characterized by factors not reasonably predictable which are known to one of ordinary skill in the art, more evidence is required to show possession").

[8] While an example is indeed not required, lack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and undeveloped art (see rejection above as exemplified by the Taylor and Darby references). Furthermore, even if, *assuming arguendo*, Applicants did set forth a working example (which is not the case), one of ordinary skill would not necessarily expect to be able to extrapolate the disclosed example as far as its applicability to the instant claims because the art is unpredictable. That is, if one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Additionally, the Board has held on the issue of unpredictability that "... the unpredictability of an art area alone may be enough to create a reasonable doubt as to the accuracy of statements in the specification." *Ex parte Singh*, 17 U.S.P.Q.2d 1714,1716 (B.P.A.I. 1990). Here, Taylor states, for example, that there are currently "no examples of such an approach [biosynthesis of epothione]" and that while it may be "easy to imagine how novel epothione analogs could be generated", "[m]uch work

remains to be done in elucidating the organization and structure of hybrid PKSs/NRPSs, however, before combinatorial biosynthesis with these systems can be undertaken" (emphasis added) (see Taylor, S. V. in "Handbook of Combinatorial Chemistry" Eds. Nicolaou, K. C.; Hanko, R.; Hartwig, W. Weinheim Germany: Wiley-VCH 2002, Vol. 2, page 1075, last paragraph).

With respect to adequate disclosure of the scope of the presently claimed generic applicant is referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding disclosure. For adequate disclosure, like enablement, requires representative examples which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that applicant had possession of the full scope of the claimed invention. See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure. Again, Applicants provide no working examples and their claims encompass a broad genus of methods in an unpredictable art.

[9] The Examiner respectfully disagrees. In *University of Rochester v. G.D. Searle & Co., Inc.* (U.S. Court of Appeals Federal Circuit (CAFC) 358 F.3d 916, 69 USPQ2d 1886 (Fed.Cir.2004)), a method for selectively inhibiting PGHS-2 enzymatic activity failed to meet the written description requirement because the patent "neither disclose[d] any such compound nor provide[d] any suggestion as to how such a compound could be made or otherwise obtained

other than by trial-and-error research." *Id.* at 2 (quoting *University of Rochester versus G.D. Searle and Co., Inc.*, 249 F.Supp.2d at 220). Here, just because Applicants are not claiming a "specific utility" in the present case does not change the fact that "trial-and-error" research would still be required to identify and/or produce a "useful" compound. In fact, the present case is even more egregious than *Rochester* because Applicants have also failed to provide a "starting point" for the search. That is, in *Rochester* a person of skill in the art would at least know to search for compounds with selective PGHS activity. Here, Applicants do not even provide this meager morsel of guidance. Applicants do not set forth any procedure that will necessarily lead to the discovery or production of a useful compound, nor do they identify any particular class of compounds that will be more suitable than others in this respect (i.e., more likely to possess a useful biological property). *Cf. Herschler*, 591 F.2d at 701 (finding that "the array of information supplied by appellant ... [would] teach one having ordinary skill in this art that one of the class of steroids *will operate* in the claimed process") (emphasis added); *Edwards*, 568 F.2d at 1354 (description of process for making claimed compound was adequate, since described process "will inherently produce ... the claimed compound"). Thus, Applicants have clearly failed the *Rochester* test, which is directly applicable to the present case.

Accordingly, the written description rejection cited above is hereby maintained.

5. Claims 1-3 and 5-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for ***any*** of Applicants' currently claimed embodiments. Applicants have not provided ***any*** examples and, as a result, a person of skill in

the art would not know how to practice the claimed invention to produce a "useful" result without undue experimentation. This is an enablement rejection.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". Some of these factors may include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the level of one of ordinary skill;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

See *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1-2) The breadth of the claims and the nature of the invention: Applicants' claims are directed to a broad genus of methods for the combinatorial biosynthesis of unspecified compounds. Here, Applicants provide no structural limitations for the "starter units", "handles" and "solid supports" used in conjunction with the method. In addition, Applicants biosynthetic enzymatic machinery includes an unknown number of enzymes and/or enzymatic machinery system constituents drawn to the modified polyketide synthetases, natural and modified peptide synthetases, natural and modified terpene synthases and natural and modified animal fatty acid synthases (e.g., see newly amended claim 1). Furthermore, no limitations are provided for the "synthetic organic chemistry" that is further used to diversify the biosynthetic products (e.g., see claim 1, step d). Thus,

Applicants are claiming virtually an infinite number of methods for producing virtually an infinite number of compounds. Consequently, the nature of the invention cannot be fully determined because the invention has not been defined with particularity.

(3 and 5) The state of the prior art and the level of predictability in the art: While combinatorial biosynthesis has been known for some time, there are no examples of "solid phase" combinatorial biosynthesis. Therefore, the Examiner contends that the level of predictability in the art is low or absent.

A person of skill in the art would not know how to pick "solid supports" and/or "handles" that would insure a reaction between a "biosynthetic enzymatic machinery system" and modified "starter units" (e.g., see Dalby, page 1, lines 15-20, "However, the use of enzymes in the synthesis of complex molecules is currently hindered by the time taken to discover or develop an enzyme with the required substrate specificity ... identifying a suitable biocatalyst is ***extremely difficult***, as the known enzymes often do not show activity towards the desired substrate"; see also lines 27-28, "it is much more difficult to find an ... enzyme with activity towards a particular substrate, due to the high substrate specificity exhibited by most natural enzymes"; see also page 17, paragraph 1 wherein the narrow substrate specificity for transketolase is set forth that would presumably fall within the scope of Applicants' claims because it is useful in producing polketides). Furthermore, while the art shows that in some cases the "biosynthetic enzymatic machinery" has relaxed specificity and thus could accommodate a wider array of substrates, it does not show that the enzymes could accommodate substrates on a solid support like a bead or a chip. How would a "support bound starter unit" get transferred

from one enzyme to the next in the modular biosynthetic enzymatic machinery when it is bound to a reaction bead?

Furthermore, combinatorial biosynthesis is a new and highly unpredictable field that requires identification/characterization of the "modular biosynthetic enzymatic machinery." With the exception of polyketides and nonribosomally produced peptides and carbohydrates, this has not been done.

Finally, Applicants have not set forth any "screening" steps that might otherwise allow a person of skill in the art to pick out a "useful" compound from the large number of compounds that would undoubtedly be generated in a combinatorial process.

(4) The level of one of ordinary skill: The level of skill required would be high, most likely at the Ph.D. level.

(6-7) The amount of direction provided by the inventor and the existence of working examples: Applicants have not provided a single working example of this method with any specificity. For example, the specification does not disclose reagents and products that are essential for the method including examples of a "support bound starter unit", "template structure", "species of template structure after functionalization", "nonnatural natural product", "antibody recognition element" (e.g., see Applicants' response, Paper No. 19, page 2, "Applicants have not specified any species of solid support unit through out the specification and the claims"; see also page 3, paragraph 1, "Applicants have not indicated in the specification or claims any species of template"; see also page 3, paragraph 4, "Applicants have not indicated in the specification or claims any particular species of template after functionalization"; see also page 4, last paragraph, "Applicants

have not indicated in the specification or claims any particular species of nonnatural natural product") (emphasis added).

(8) The quantity of experimentation needed to make or use the invention base on the content of the disclosure: As a result of the broad and unpredictable nature of the invention and the lack of specific guidance from the specification, the Examiner contends that the quantity of experimentation needed to make and or use the invention would be great. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. In re Vaeck, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 * n.23 (Fed. Cir. 19991). In this case, Applicants have not provided any working examples that would teach a person of skill in the art "how to make" this enormous genus that falls within a highly unpredictable art area. Likewise, the specification fails to teach a person of skill in the art "how to use" this enormous genus because no "screening" steps are disclosed that would lead a person of skill in the art to a "useful" compounds. Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

Response

6. Applicant's arguments directed to the above Enablement rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for

the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

[1] Applicants state, "[we] hereby reiterate[ ] all the arguments made above in the ... Written Description response" (e.g., see 11/25/05 Response, page 9, sections (1-2)).

[2] Applicants argue, "it is well with[in] the knowledge and skill of one of ordinary skill in the art to determine whether a particular enzyme has such stringent specificity such that it will not recognize the particular starter unit that the practitioner has himself or herself chosen. That is, the practitioner is not operating in a vacuum. By choosing a desired starter unit or units, one of ordinary skill in the art would know which enzyme or enzymes may use those particular starter units as catalytic substrates" (e.g., see 11/25/05 Response, page 10, paragraph 1).

[3] Applicants argue, "[t]he Examiner concedes that tee prior at shows that, in some cases, the biosynthetic enzymatic machinery has relaxed specificity and thus could accommodate a wide array of substrates." (e.g., see 12/25/05 Response, page 10, middle paragraph).

[4] Applicants argue, "[we have] disclosed that researchers have made various modifications to certain preferred biosynthetic enzymes that alter their catalytic properties, indicating that those skilled in the art are not only able to generally identify the substrate specificity of a given biosynthetic enzymatic machinery system, but are in fact able to specifically engineer variants of these enzymes with altered substrate specificity ... Thus, far from being an unpredictable field, as the Examiner asserts, specific examples of combinatorial biosynthesis are well known to those of ordinary skill in the art" (e.g., see 11/25/05 Response, paragraph bridging pages 10 and 11).

[5] Applicants argue, "[f]or reasons largely identical to those given above in the Working Examples section of the Written Description response, Applicant submits that the specification does in fact provide adequate enablement support" (e.g., see 11/25/05 Response, page 11, sections (6 and 7).

[6] Applicants argue, "the Examiner has not appreciated the novelty and utility of the claimed methods since none of these disclosed reagents and/or products are in fact essential for practicing the claimed methods" (e.g., see 11/25/05 Response, page 12, paragraphs 1 and 2).

[7] Applicants argue, "[f]or the reasons presented above in the Working examples section of the Written Description response, Applicant disagrees" (e.g., see 11/25/05 Response, page 12, section (8)).

[8] Applicants argue, "[t]he fact that the practitioner may need to perform routine experiments to determine which enzymes and/or functionalization reactions to utilize when practicing the claimed invention does not mean that the art is highly unpredictable" (e.g., see 11/25/05 Response, page 13, first full paragraph).

This is not found persuasive for the following reasons:

[1, 5 and 7] To the extent that Applicants are simply "reiterating" their previous arguments, the Examiner contends that those issues were adequately addressed in those previous sections, which are incorporated in their entirety herein by reference.

[2] The Federal Circuit has cautioned against over reliance on the assertion that everything needed to practice the full scope of the claims was known in the art. See *Genentech Inc. v. Novo Nordisk* A/S, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997) ("[T]hat general, oft-repeated statement [that a patent need not teach, and preferably omits, what

is well known in the art] is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. ... It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement"). Here, Applicants have not provided any utility for the vast number of claimed compounds (see rejection above). In addition, Applicants have not provided any basic reaction schemes that would enable a person of skill in the art to produce the vast majority of the claimed compounds regardless of whether or not basic organic chemistry principles or relaxed enzymes would permit such a synthesis if it were to be discovered by someone other than the inventors in the future. Thus, these omissions represent more than just "minor" details.

The Genentech court also held that, "[w]hile every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." Id. In this case, as in *Genentech*, the specification does not provide the "reasonable detail . . . to enable members of the public to understand and carry out the invention." It therefore does not satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph.

[3] As stated in the rejection above, while the art shows that in some (limited) cases the "biosynthetic enzymatic machinery" has relaxed specificity and thus could accommodate a wider array of substrates, it does not show that the enzymes could accommodate substrates on a solid support like a bead or a chip. Moreover, applicant's arguments that the starter units will be transferred in the "same" manner do not rise to the level of factual evidence. See MPEP § 716.01(c): The arguments of counsel cannot take the place of evidence in the record. *In re*

Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Thus, Applicants have not refuted in any way the Examiner's position that the art is unpredictable and a person of skill in the art would not expect the "same" type of reaction for all of the currently claimed enzymes. As noted above, a person of skill in the art would not know how to pick "solid supports" and/or "handles" that would insure a reaction between a "biosynthetic enzymatic machinery system" and modified "starter units" (e.g., see Dalby, page 1, lines 15-20, "However, the use of enzymes in the synthesis of complex molecules is currently hindered by the time taken to discover or develop an enzyme with the required substrate specificity ... identifying a suitable biocatalyst is ***extremely difficult***, as the known enzymes often do not show activity towards the desired substrate"; see also lines 27-28, "it is much more difficult to find an ... enzyme with activity towards a particular substrate, due to the high substrate specificity exhibited by most natural enzymes"; see also page 17, paragraph 1 wherein the narrow substrate specificity for transketolase is set forth that would presumably fall within the scope of Applicants' claims because it is useful in producing polketides). Here, Applicants have simply failed to refute, or even respond to, the Dalby reference.

[4] The Examiner respectfully disagrees. Nothing in Applicants' specification provides any evidence that the "known" biosynthetic enzymatic machinery will react favorably with the currently claimed starter units/functional handles. In addition, Applicants failed to address the Taylor reference showing that the art is not predictable. For example, Taylor states that for the biosynthesis of epothione would require a mixed NRPS/PKS "biosynthetic enzymatic machinery." However, Taylor states that there are currently "no examples of such an approach [in the literature]" and that while it may be "easy to imagine how novel epothione analogs could

be generated", "[m]uch work remains to be done in elucidating the organization and structure of hybrid PKSs/NRPSs, however, before combinatorial biosynthesis with these systems can be undertaken" (emphasis added) (see Taylor, S. V. in "Handbook of Combinatorial Chemistry" Eds. Nicolaou, K. C.; Hanko, R.; Hartwig, W. Weinheim Germany: Wiley-VCH 2002, Vol. 2, page 1075, last paragraph). Therefore, Applicants are clearly not enabled for systems like PKS/NRPS wherein the "biosynthetic enzymatic machinery" has not yet been characterized.

Furthermore, Applicants' arguments do show "how to use" the compounds that can be produced by the method. That is, even if, *assuming arguendo*, the full scope of the compounds could be made (which is not the case), there is no evidence that the vast majority of these compounds would be useful. It is well settled from *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991), that a patent applicant is entitled to claim an invention generically if the invention is described sufficiently to meet the requirements of 35 U.S.C. § 112. In *Amgen*, the applicant claimed erythropoietin (EPO), and every possible analog of the gene (containing about 4000 nucleotides), but only provided the details for preparing only a few EPO analogs and did not provide sufficient disclosure to support the claims. The CAFC held that in view of the structural complexity of the EPO gene, there were manifold possibilities for changes in its structure, and there was uncertainty as to what utility would be possessed by each of the analogs. It was determined that additional disclosure was needed to identify various analogs within the scope of the claim, methods for making them, and structural requirements for producing compounds with EPO-like activity.

In the present case, Applicants have similarly failed set forth any utility for the vast number of compounds produced by the currently claimed method. "Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable ... *Genentech, Inc. v. Novo Nordisk*, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997). Tossing out the mere germ of an idea does not constitute enabling disclosure. See, *Brenner v. Manson*, 383 U.S. 519, 536 ; 148 USPQ 689, 696 (1966) (stating, in context of the utility requirement, that `a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.')"). Applicants' disclosure provides merely an invitation to those of skill in the art to determine how to use the compounds that can be produced by the currently claimed methods presumably using assays that are known in the prior art.

[6] The Examiner respectfully disagrees. While no specific reagents may be "required" to make "useless" compounds, specific reagent would certainly be required to make "useful" ones. Any other interpretation would be inconsistent with §§ 101 and 112 of the statute.

[8] The Examiner has never contended that routine experiments impart a high level of unpredictability to the currently claimed invention. In contrast, the Examiner states that the art is unpredictable for the reasons set forth in the above reject as evidenced by the Dalby and Taylor references. Again, Applicants failed to address both references. For example, Dalby states, "... the use of enzymes in the synthesis of complex molecules is currently hindered by the time taken to discover or develop an enzyme with the required substrate specificity ... identifying a suitable biocatalyst is ***extremely difficult***, as the known enzymes often do not show activity towards the desired substrate" (see Dalby, page 1, lines 15-20; see also lines 27-28, "it is much more difficult

to find an ... enzyme with activity towards a particular substrate, due to the high substrate specificity exhibited by most natural enzymes"; see also page 17, paragraph 1 wherein the narrow substrate specificity for transketolase is set forth that would presumably fall within the scope of Applicants' claims because it is useful in producing polketides). Thus, the Examiner has met the "initial burden" of "setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application" in accordance with *In re Wright*, 999 F.2d 1557, 1561-62, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

Additionally, the specification fails to describe how to test compounds and also fails to specify which compounds would be more likely to produce a favorable result. In fact, Applicants claims do not even require a "screening" step (see rejection above) and, as a result, the vast majority of compounds produced by the method would be useless. Furthermore, only "trial-and-error" research could be used to determine which compounds, if any, might produce a useful result.

Accordingly, the Enablement rejection cited above is hereby maintained.

7. Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention. This is a new matter rejection.

A. In newly amended claim 7, to the extent that removal of the phrase "chemically robust" extends beyond the "robust" handles (i.e., reads on non-robust and robust), the

increased breadth of possible modification constitutes new matter, since there is no specification support or original claim support for such scope; nor has applicant provided any indication where such support exists.

Response

8. Applicant's arguments directed to the above New Matter rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicant argues, "The Examiner seems to be saying that the Applicant is limited to claiming preferred embodiments described in the [original] specification. However, this is not the law" (e.g., see 11/25/05 Response, pages 13 and 14).

This is not found persuasive for the following reasons:

The Examiner has never argued that Applicants should be limited to their "preferred" embodiments as erroneously purported. The general test for determining whether later claimed subject matter is supported by an earlier written description is whether the disclosure of the application "reasonably conveys to a person skilled in the art that the inventor had possession of the claimed subject matter at the time of the earlier filing date." *Eiselstein v. Frank*, 52 F.3d 1035, 1039, 34 USPQ2d 1467, 1470 (Fed. Cir. 1995); *Ralston Purina Co. v. Far-Mar-Co., Inc*, 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985). The specification must provide information that clearly allows persons having ordinary skill in the art to recognize that the

applicant invented the later claimed subject matter. In re *Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

The Federal Circuit has analogized the determination of whether there is written descriptive support in a specification to following a trail through the forest by looking for "blaze marks" on individual trees:

> Many years ago our predecessor court graphically articulated this standard by analogizing a genus and its constituent species to a forest and its trees. As the court explained:
>
> > It is an old custom in the woods to mark trails by making blaze marks on the trees. It is no help in finding a trail . . . to be confronted simply by a large number of unmarked trees. Appellants are pointing to trees. We are looking for blaze marks which single out particular trees.

Fujikawa v. Wattanasin, 93 F.3d 1559, 1570, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996), quoting *In re Ruschig*, 379 F.2d 990, 994-95, 154 USPQ 118, 122 (CCPA 1967). "Precisely how close the original description must come to comply with the description requirement of Section 112 must be determined on a case-by-case basis." *Eiselstein*, 52 F.3d at 1039, 34 USPQ2d at 1470, quoting *Vas-Cath*, 935 F.2d at 1561, 19 USPQ2d at 1116, quoting *In re Smith*, 481 F.2d 910, 914, 178 USPQ 620, 623-24 (CCPA 1973).

The determination that newly added subject matter meets § 112's written description generally involves at least one of three factors. The first involves the situation where claimed language is literally stated in the specification, (i.e., literal antecedence in the specification for the newly added subject matter). The description requirement is ordinarily met by a specification that describes the invention in the same words as the claims. *In re Bowen*, 492 F.2d 859, 864, 181 USPQ 48, 52 46 (CCPA 1974). See also, *Snitzer v. Etzel*, 465 F.2d 899, 902, 175 USPQ 108, 110-11 (CCPA 1972), appeal after remand, 531 F.2d 1062, 189 USPQ 415 (CCPA 1976); *Martin*

v. Johnson, 454 F.2d 746, 751-52, 172 USPQ 391, 395 (CCPA 1972). Here, Applicants have failed to provide literal support for "non-robust" handles. The original specification and claims only provide literal antecedence for "chemically robust" handles (e.g., see Applicants' cited passage at page 8, lines 17-19). If applicant believes this rejection is in error, applicant must disclose where in the specification support for this amendment can be found in accordance with MPEP 714.02. This has not been done.

If the new limitation is not literally set forth, then it must next be determined whether the limitation was actually described although in different language. *In re Wilder*, 736 F.2d 1516, 1520, 222 USPQ 369, 372 (Fed. Cir. 1984) ("It is not necessary that the claimed subject matter be described identically . . . ."); *In re Lukach*, 442 F.2d 967, 968-69, 169 USPQ 795, 796 (CCPA 1971). (The written description requirement does not require in haec verba antecedence in the originally filed application). However, where different language is relied upon for support, "the specification must contain an equivalent description of the claimed subject matter." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); Wagoner v. Barger, 463 F.2d 1377, 1380, 175 USPQ 85, 86 (CCPA 1972). Here, Applicants have not pointed to any "equivalent" language that would encompass "non-robust" handles.

Last, if neither explicit language nor equivalent language is present, then it must be determined if the newly claimed feature is inherently present in the specification. *Therma-Tru Corp. v. Peachtree Doors Inc.*, 44 F.3d 988, 993, 33 USPQ2d 1274, 1276 (Fed. Cir. 1995) ("[T]he later explicit description of an inherent property does not deprive the product of the benefit of the filing date of the earlier application."). Proof of inherency requires evidence that the "necessary and only reasonable construction to be given the disclosure by one skilled in the

art is one which will lend clear support to . . . [this] positive limitation. . . ." *Kennecott Corp. v. Kyocera International Inc.*, 835 F.2d 1419, 1423, 5 USPQ2d 1194, 1198 (Fed. Cir. 1987) quoting *Langer v. Kaufman* , 465 F.2d 915, 918, 175 USPQ 172, 174 (CCPA 1972) quoting *Binstead v. Littmann* , 242 F.2d 766, 770, 113 USPQ 279, 282 (CCPA 1957). In *Kennecott*, 835 F.2d at 1423, 5 USPQ2d at 1198, the court noted:

> The court has generally applied this standard of the "necessary and only reasonable construction" as a basis for determining whether an application could, on the basis of an inherent property, support a limitation in an interference count. [Citations omitted.]

As noted by the CCPA:

> Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient. [Citations omitted.] If, however, the disclosure is sufficient to show that the natural result flowing from the operation as taught would result in the performance of the questioned function, it seems to be well settled that the disclosure should be regarded as sufficient.

In re Oelrich, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981), quoting, *Hansgirg v. Kemmer*, 102 F.2d 212, 214, 40 USPQ 665, 667 (CCPA 1939). Thus, it is not sufficient that a person following the disclosure might obtain the result set forth; it must inevitably happen. *Dreyfus v. Sternau*, 357 F.2d 411, 415, 149 USPQ 63, 66 (CCPA 1966); Crome v. Morrogh, 239 F.2d 390, 392, 112 USPQ 49, 50 (CCPA 1956). Here, the specification does not "inevitably" set forth non-robust handles. To the contrary, "chemically robust" handles are also set forth.

Accordingly, the New Matter rejection cited above is hereby maintained.

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114.

See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
May 13, 2006

JON EPPERSON, PH.D.
PATENT EXAMINER